Applicants respectfully submit that the Action has not established a factual basis to support the rejection under 35 U.S.C. § 103(a). The Action has not set forth an articulated reasoning or rationale for the position that the features that are not disclosed in the cited patents would have been obvious to one skilled in the art. The conclusory statements in the Action without evidence to support the conclusions is not sufficient to support a prima facie case of obviousness.

The rejection concludes that the features recited in the claims are nothing more than an optimization. However, the Action provides no factual basis that the claimed features are known in the art to be optimum values or that the features are routinely modified to obtain an optimization. Nothing in the art of record suggests that one skilled in the art would recognize that the claimed features could or should be "optimized" and that "optimizing" the features would obtain the benefits of the claimed invention. Thus, the rejection is based entirely on speculation and not on any evidence of record.

DE '585 and Beam et al. were cited in the previous rejection, which is now withdrawn. For the reasons discussed below, Starling et al. clearly does not provide the deficiencies of DE '585 and Beam et al. The Action contends that the claimed pore shape, particle size range and interconnecting pore share are nothing more than routine optimization. DE '585, Beam et al. and Starling et al. provide no suggestion to one skilled in the art that these features are matters of routine optimization as asserted in the Action. Moreover, the Action does not identify where the art of record allegedly supports this conclusion.

For the reasons discussed in the previous response, DE '585 and Beam et al. fail to disclose or suggest the features of the claimed invention. For example, DE '585 clearly does not disclose or suggest the claimed bone formation agent having an interconnecting pore share where the porosity "is limited to pore sizes less than 10 μm" as in claim 1. Thus, claim 1 specifically limits the interconnecting pores to have a pore size of less than 10 μm thereby

excluding the pores of the cited patents. The art of record specifically requires the macropores to be the interconnecting pores. DE '585 specifically discloses the interconnecting macropores as being essential to the temporary bone defect filler. See, for example, page 6, lines 1-7, of the English translation of DE '585. DE '585 specifically teaches that the interconnecting macropores are essential for the rapid boney ingrowth of the implant. Thus, DE '585 effectively teaches away from the claimed invention of having interconnecting pores that are less than 10 μm.

The Action provides no factual evidence to support the assertion that it is known by one skilled in the art that modifying the interconnecting pore size is a known means for optimizing the composition. Moreover, it would not have been obvious to one skilled in the art to modify the interconnecting pore size in a manner that is contrary to the express disclosure of DE '585. It would not have been obvious to eliminate the one aspect of DE '585 that is expressly disclosed as being essential. There is no evidence to support the assertion that one skilled in the art would have a reasonable expectation of success in modifying DE '585 as suggested in the Action.

The absence of the interconnecting macropores of DE '585 would not be effective for the intended use of DE '585. The resulting product would not enable the rapid boney ingrowth as specifically desired by DE '585. The Action provide no factual basis for the position that it would have been obvious to disregard the essential aspect of DE '585 with a reasonable expectation of success. By eliminating the essential aspect of DE '585, one skilled in the art would clearly have no reasonable expectation of success in obtaining a bone formation agent having the advantages of the present invention.

The Action cites no authority or factual basis that the claimed interconnecting pore size can or should be modified contrary to the teaching of DE '585. The Action provides no rational basis to establish the motivation or reason why one skilled in the art would change

the interconnecting pore size of DE '585, that the interconnecting pore size can or should be altered or that there is a legitimate reasons for modifying the interconnecting pore size of DE '585.

The Action further asserts that the claimed particle size is nothing more than a routine optimization but provides no factual evidence to support the assertion. The Action provides no evidence to suggest that changing the particle size is a known means for optimizing a bone growth implant. The Action further provides no evidence to suggest that one skilled in the art would be motivated to change the particle size of the cited patents. DE '585 discloses the particle size being about 1.5 times greater than the claimed amount. The Action provides no factual basis or rationale to support the assertion that it would have been obvious to one skilled in the art to modify the particle size as claimed.

The Action also provides no evidence to support the assertion that the shape is a "preferential choice" which can be optimized. The Action provides no rationale to support the assertion that the shape of the macropores is a known means for optimizing the bone growth implant. The Action further fails to provide any evidence that the claimed statistically distributed pores are known by those skilled in the art to be a routine optimization. Thus, the assertion in the Action is not based on any factual evidence and instead is based on speculation.

Beam et al. is cited for disclosing a bimodal pore size where the structure can be isotropic. The Action provides no basis for the position that it would have been obvious to modify DE '585 according to Beam et al. Furthermore, Beam et al. does not disclose granules or shaped particles formed from granulates having the claimed statistically distributed porosity with the pore size ranges of claim 1. Beam et al. further fails to disclose interconnecting pores where the pore size is less than 10 μm. In contrast, Beam et al.

specifically discloses the interconnecting meso and/or macropores. See, for example, Figures 16 and 19, and claim 1 of Beam et al.

The claimed invention specifically defines the interconnecting pores being "limited" by a porosity having a pore size less than 10 μm. Thus, the claimed invention excludes the meso and macropores of Beam et al. and the macropores of DE '585. Beam et al. is sufficiently different from DE '585 that it would not have been obvious to one skilled in the art to modify the filler of DE '585 according to Beam et al. Moreover, it would not be technically possible to modify DE '585 or the resulting product according to Beam et al. to achieve an isotropic structure. Beam et al. does not disclose granulates or shaped articles formed from granulates having a statistically distributed porosity with the discrete pore size ranges as claimed. Beam et al. relates to a regular biostructure referred to as an engineered shaped article. In contrast, the present invention is directed to granulates or shaped pieces formed from the granulates having a statistical pore size distribution, polygonal shaped pores as well as polygonal shaped granulates.

Beam et al. does not disclose the discrete pore size ranges or the interconnecting pores limited to a pore size of less than 10 μm as in the claimed invention. Beam et al. does not disclose the porosity having an irregular geometric shape where the sintered particles of calcium phosphate have a particle size smaller than 63 μm and a D50 value in the range of 5 to 20 μm. Thus, even if one were to combine the teachings of Beam et al. and DE '585, the result would not be the claimed invention. Starling et al. relates to hollow calcium phosphate microbeads or microspheres and the use of the microbeads or microspheres in the cell culturing system and for chromatography and implantable biomedical materials. Starling et al. provides no suggestion to one skilled in the art that changing the pore size is a known means of optimizing the pore size as asserted in the Action. Moreover, Starling et al. clearly provides no suggestion to one skilled in the art to modify the pore size of DE '585 in a

manner contrary to the specific teachings of DE '585. DE '585 does not teach the desirability of modifying the pore size within the claimed range. Thus, merely because Starling et al. discloses that various process steps have an effect on the pore size does not render the claimed invention obvious. Starling et al. does not teach the desirability of modifying the pore size. Thus, the Examiner's conclusion of obviousness is not supported by any reasonable basis in the art of record as to the desirability of the claimed pore size.

Starling et al. does not disclose a bone forming agent having an isotropic sintered structure with two discrete pore sizes, a particle size smaller than 63 μm with interconnecting pores with a pore size of less than 10 μm as in the claimed invention. In contrast, Starling et al. discloses microspheres having a particle size range of about 500 μm to about 1,000 μm in diameter and having an interstitial open porosity of about 60% with a pore size range of about 350 μm to about 500 μm used for an implantable calcium phosphate microsphere. See, for example, column 8, line 57, to column 9, line 5, of Starling et al.

Starling et al. specifically discloses the pore size of 350 μm to 500 μm to facilitate the bone ingrowth. See, for example, column 11, lines 56-60. Thus, Starling et al. effectively teaches away from the claimed invention.

Furthermore, Starling et al. distinguishes between the closed porosity, i.e., the pores within the microspheres that are not open to the external surface as disclosed in column 7, lines 11-20, and open porosity which refers to the porosity between the bonded and aggregated microbeads referred to as the interstitial open porosity.

Starling et al. discloses that the surface of the hollow microsphere can be altered by applying a porous layer of a suitable particulate calcium phosphate ceramic. The coating is referred to as a cap coating or porous cap. The coating is provided to increase the chemical activity of the microbeads due to the higher surface area and to the large interconnecting pore size in the coating forming porous channels to accommodate cell and tissue ingrowth. See

Example 3 of Starling et al. In contrast to the present invention, the pore size distribution of Starling et al. in the resulting coating is not statistically distributed pores but instead are regular due to the conventional spherical form of the microbeads that form the aggregate with the open porosity. See, for example, Figure 1 and the microspheres 1.0, 1.4 and 1.8. In addition, the open porosity of the materials of Starling et al. is limited to a single pore size. In contrast, the claimed invention is a bone formation agent having at least two discrete pore sizes.

In Examples 6 and 10 of Starling et al., there is no indication of the pore size. Thus, Examples 6 and 10 do not disclose or suggest the claimed bone formation agent of claim 1.

Starling et al. does not teach or suggest a bone formation agent without interconnecting macropores. Starling et al. also fails to disclose or suggest a bone formation agent having statistically distributed pores, a porosity composed of at least two discrete pore size distributions and pores of an irregular geometric shape. Starling et al. clearly provides no motivation or incentive to one skilled in the art to modify the products of DE '585 or Beam et al. as suggested in the Action. Regardless of whether Starling et al. discloses that the pore size can be changed by changing the process conditions, Starling et al. clearly fails to teach the desirability of doing so. Prima facie obviousness is not established by showing that one skilled in the art is capable of making the modification when there is no teaching or suggestion or common knowledge in the art of making the proposed modification.

Contrary to the present invention, Starling et al. teaches that microspheres for use as biomedical implants preferably have a particle size of about 500 to 1,000 μm in diameter and a pore size in the range of about 350 to 500 μm. Even if one were to combine the teachings of Starling et al. with Beam et al. and DE '585, the resulting product would not be a bone formation agent having a porosity of (1) at least two discrete pore size distributions, (2) an

absence of interconnecting macropores, and (3) interconnecting pores being micropores having a diameter of less than 10 μm.

In view of the above comments and the deficiencies of the cited patents, claim 1 would not have been obvious to one skilled in the art over the combination of DE '585, Beam et al. and Starling et al. Accordingly, Applicants respectfully submit the rejection should be withdrawn.

The Action has not established a reasonable basis that one of ordinary skill in the art would have a reasonable expectation of success in obtaining the properties of the claimed bone formation agent. The combination of the cited patents effectively teach away from a bone formation agent having interconnecting micropores within the claimed range. Each of the cited patents require interconnecting macropores. Claim 1 excludes the interconnecting macropores of the cited patents by limiting the interconnecting pores to a pore size of less than 10 μm.

The dependent claims are also allowable as being dependent from an allowable base claim. The combination of the cited patents do not disclose the two discrete pore size distributions of claim 2, the granular size of claim 7, the average granular size of claim 12, the shaped body of claim 13, the statistical porosity of claim 14, the tubular porosity having bores with a diameter of 0.5 to 2 mm as in claim 15, the additional component on the surface of the bone formation agent of claim 17, the shape of the bone formation agent of claim 18, the dimensions of claim 19, or the shape of claim 20, in combination with the features of claim 1.

Claims 3, 4, 11, 12 and 16 are rejected under 35 U.S.C. § 103(a) as being obvious over DE '585, Beam et al., Starling et al., and further in view of WO 92/21302. WO '302 is cited for disclosing an implant made of a porous material having three pore sizes.

WO '302 does not provide the deficiencies of DE '585, Beam et al. and Starling et al. Specifically, WO '302 does not disclose interconnecting micropores having a pore size of less than 10 μm. Furthermore, WO '302 specifically discloses the pores being distributed in different parts of the implant. There is no disclosure of three distinct pore sizes in the particles as in the claimed invention. WO '302 does not suggest three distinct pore size distributions having pore diameters in the range of 0.5 to 10 μm, 10 to 100 μm and 100 to 5,000 μm where the particles have interconnecting pores limited to less than 10 μm as in the claimed invention. Thus, it would not have been obvious to one of ordinary skill in the art to provide a bone formation agent with the claimed discrete pore size distribution.

The cited patents do not suggest to one skilled in the art the pore size distribution of claim 3, the pore size distribution having 0.5 to 10 μm and 5 to 40% by volume at a pore size distribution with a pore diameter of 10 to 100 μm and 1 to 40% by volume of a pore size distribution with pore diameters of 100 to 5,000 μm with an overall porosity not exceeding 85% by volume as in claim 4, either alone or in combination with the features of claim 1. WO '302 specifically discloses that not more than 5% of the pore size is in the range of 10 to 50 μm. The claimed pore size distribution having a pore diameter in the range of 0.5 to 10 μm define the interconnecting pore system. WO '302 does not disclose or suggest this feature. Accordingly, claim 4 is not obvious over the cited patents.

The cited patents also do not disclose the maxima of the discrete pore distribution of claims 11 and 12, or the pore distribution of claim 16, in combination with the features of claim 1. Accordingly, the claims are not obvious over the combination of the cited patents.

Claims 5, 8-10 and 18-20 are rejected under 35 U.S.C. § 103(a) as being obvious over DE '585, Beam et al., Starling et al., WO '302 and U.S. Patent No. 6,521,246 to Sapieszko et al. Sapieszko et al. is cited for disclosing inorganic shaped bodies for bone grafting.

Sapieszko et al. does not provide the deficiencies of DE '585, Beam et al. and Starling et al. Sapieszko et al. relates to inorganic shaped bodies for beta-tricalcium phosphate having a porosity of 30 to 90%. Sapieszko et al. discloses the pores being uniform and being produced according to a template technique using a sponge as a substrate. The sponge is imbibed with a reaction solution containing calcium phosphate. The organic component of the sponge is burned to produce the calcium phosphate framework corresponding to the pores in the sponge. The pores of the sponge generally have round shapes as shown in the Figures of Sapieszko et al.

Sapieszko et al. does not disclose the calcium phosphate containing 95% of alpha-tricalcium phosphate, beta-tricalcium phosphate, octa-calcium phosphate, alkali metal modified and/or alkaline earth metal-modified tricalcium phosphate, calcium diphosphate, carbonate apatite of type B, calcium-deficient hydroxyapatite or mixtures thereof as in claim 5, in combination with the features of claim 1. Sapieszko et al. further fails to disclose the geometric shapes of claims 8-10, the discrete pore size distribution of claims 11 and 12, the shaped body of claims 13-15, the pore size distribution of claim 16, the surface component of claim 17, or the shaped body of claims 18-20, in combination with the features of claim 1. Accordingly, the claims are not obvious over the combination of the cited patents.

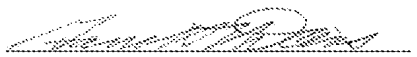
Claim 6 is rejected under 35 U.S.C. § 103(a) as being obvious over the combination of DE '585, Beam et al., Starling et al., WO '302, Sapieszko et al. and further in view of Trisi et al. The combination of the six cited references does not render claim 6 obvious to one of ordinary skill in the art.

Trisi et al. is cited for disclosing pure phase beta-tricalcium phosphate. Trisi et al. provides no suggestion to one skilled in the art to use beta-tricalcium phosphate having a phase purity of greater than 99% by weight in a bone formation agent of claim 1. The Action provides no basis for the position that it would have been obvious to use the beta-tricalcium

phosphate of Trisi et al. in the structure of DE '585. For the reasons discussed above, even if one were to do so, the resulting combination would not be the claimed invention. Accordingly, claim 6 is not obvious over the combination of the cited patents.

In view of the above comments, Applicants respectfully submit that the claims are in condition for allowance. Accordingly, reconsideration and allowance are requested.

Respectfully submitted,



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